Claims

1. A method for synthesising a bifunctional complex comprising a template-directed molecule and a template for the synthesis thereof, the method comprising the steps of:

a) providing a template comprising two or more codons in sequence, a first part of a molecular affinity pair, and a reactive group,

b) providing two or more building blocks, each building block comprises

i) an anti-codon capable of recognising a codon of the template,

ii) a functional entity comprising at least one reactive group,

iii) a linker connecting the anti-codon and the functional entity,

wherein building blocks having anti-codons intended to interact with codons of the template distal to the reactive group comprise as a section of the linker a second part of the molecular affinity pair,

c) contacting the template with a building block under conditions which allow specific hybridisation of the anti-codon of the building block to the codon of the template, and under conditions ensuring assembling of the parts of the molecule pair, if present,

d) obtaining a connection between the functional entity of the building block and the template by a reaction involving the template reactive group and the functional entity reactive group,

e) cleaving a linkage to obtaining a nascent templated molecule,

f) separating the parts of the molecular affinity pair,

g) repeating, for a building block having an anti-codon capable of hybridising to a new codon, steps c) to f) one or more times,

2. The method according to claim 1, wherein the first part of the affinity pair is capable of reversible interaction with the second part of the affinity pair.

3. The method according to claim 1 or 2, wherein the first part of the affinity pair is a sequence of nucleotides and the second part of the affinity pair is

a sequence of nucleotides capable of hybridising to the first part of the affinity pair.

4. The method according to claim 1 or 2, wherein the one or more at the nucleotides of the second part of the affinity pair comprise a non-specific base-pairing nucleobase.

5. The method according to claim 4, wherein the non-specific pairing nucleobase is selected from the group comprising inosine, pyrene, 3-nitropyrrole, N^8-8aza-7deazaadenine and 5-nitroindole.

6. The method according to claim 1, wherein the first part of the molecular affinity pair is comprised by the two or more of the codons in sequence.

7. The method according to claim 1, wherein the codon is a sequence of nucleotides.

8. The method according to claim 1, wherein the nucleotide sequence of the first part of the molecular affinity pair comprise at least a part of the nucleotide sequence of the codon proximal to the reactive group of the template.

9. The method according to claim 1, wherein the reactive group of the template is covalently attached to the template.

10. The method according to claim 1, wherein the reactive group of the template is a part of a functional entity or a nascent templated molecule.

11. The method according to claim 1, wherein the reactive group of the template is a part of a scaffold.

12. The method according to claim 1, wherein the reactive group of the template is non-covalently attached to the template.

13. The method according to claim 12, wherein the reactive group of the template is attached to a sequence of nucleotides, which complements a sequence of nucleotides of the template.

14. The method according to claim 13, wherein the reactive group of the template is attached to an anti-codon complementing a further codon of the template.

15. The method according to claim 1, wherein the template comprises two regions of codons, the two or more codons in sequence of step a) belonging

to the first region and the second region of codons comprising one or more codon(s) for initial attachment of the reactive group of the template.

16. The method according to claim 1, wherein neighbouring codons of the codons in sequence are separated by a spacer group.

17. The method according to claim 16, wherein the spacer group identifies the position of a codon.

18. The method according to claim 16, wherein the spacer group comprises a sequence of one or more guanine nucleobase(s).

19. The method according to claim 1, wherein the number of codons of the template is 3 to 100.

20. The method according to any of the claims 1 to 19, wherein each codon is a sequence of 3 to 100 nucleotides.

21. The method according to claim 20, wherein the each codon comprises a sequence 3 to 30 nucleotides.

22. The method according to claim 1, wherein the second part of the molecule affinity pair in the linker of the building block is arranged proximal to the functional entity.

23. The method according to claim 22, wherein the second part of the molecular affinity pair is spaced from the functional entity by 0 to two nucleotides.

24. The method according to claim 1, wherein the reactive group of a building block functional entity is capable of forming a direct connection to a reactive group of the template.

25. The method according to claim 1, wherein the reactive group of a building block is capable of forming a connection to a reactive group of the template through a bridging fill-in group.

26. The method according to claim 1, wherein the connection and the subsequent cleavage of the linkage according to steps d) and e) results in a transfer of the functional entity to the nascent template-directed molecule.

27. The method according to claim 1, wherein the connection and the subsequent cleavage of the linkage according to steps d) and e) results in a

transfer of the nascent template-directed molecule to the to functional entity of the building block.

28. The method according to claim 1, wherein steps d) and e) occur simultaneously.

29. The method according claim 1, wherein the anti-codon, the linker and the second part of the molecular affinity pair is a contiguous linear oligonucleotide.

30. The method according to claim 1, wherein the linker is attached to the functional entity via the reactive group.

31. The method according to claims 24 to 30, wherein the functional entity comprises a further reactive group capable of participating in a repeated formation of a connection according to steps c) to f).

32. The method according to claims 26 or 27, wherein the transfer of the functional entity of step d) involves simultaneous connecting the functional entity to the template and cleavage of the junction between the functional entity and the linker.

33. The method according to any of the claims 1, wherein the contacting of the building blocks with the template involves separate addition of the individual building blocks.

34. The method according to any of the claim 1, wherein the contacting of the individual building blocks with the template is controlled by directing the annealing temperature.

35. The method according to claim 34, wherein the method comprise addition of all, or a substantial amount of, the building blocks to the template and directing the contacting by step-wise decreasing the temperature.

36. The method according to claim 1, wherein the anti-codon of a reacted building block not harbouring the nascent template-directed molecule is removed from the template prior to repetition of steps c) to f).

37. The method according to claim 36, wherein the anti-codon is removed by melting it off the template.

38. The method according to claim 36, wherein the anti-codon is at least partly digested enzymatically.

39. The method according to claim 38, wherein the anti-codon is degraded by any one of the methods selected from the group consisting of providing a DNA template and an anti-codon comprising RNA and treating the DNA:RNA duplex with an enzyme selected from RNAseH, RNAseA, RNAse 1, weak alkaline conditions (pH 9-10), or aqueous $Pb(Ac)_2$; providing a DNA template and an DNA or RNA anti-codon comprising a thiophospate in the internucleoside linker and subsequent treating with aqueous iodine; and proving a DNA or RNA template and a DNA anti-codon comprising an uracil nucleobase, treating with uracil-glycosylase and subsequent weak acid.

40. The method according to any of the claims 1 to 39, comprising the further step of connecting the templated molecule with the template which directed the synthesis thereof via a covalent link.

41. The method according to claim 40, wherein the covalent link is selectively cleavable to provide for a release of the templated molecule.

42. The method according to claim 1, wherein the templated molecule is a polymer.

43. The method according to any of the preceding claims, comprising the further step of transferring the templated molecule to an anchorage point on the template or a sequence complementing the template, to establish an effective chemical connection.

44. The method according to claim 43, wherein the complementing sequence has a higher annealing temperature than the annealing temperature of one or more of the building blocks.

45. The method according to claim 43 or 44, wherein the sequence complementing the template is covalently connected to the template.

46. The method according to claim 45, wherein the covalent link is selectively cleavable to provide for a separation of the templated molecule from the template.

47. A library of different complexes, each complex comprising a template-directed molecule and a template for the synthesis thereof, said library being obtainable by processing a plurality of different templates and a plurality of building blocks according to any of the claims 1 to 46.